BRAIN CONNECTIVITY
Volume 4, Number 9, 2014

DOI: 10.1089/brain.2014.1503

Personal Reflections on James S. Hyde

In honor of Dr. James S. Hyde's contributions to the field of functional magnetic resonance imaging (fMRI) and resting-state functional connectivity magnetic resonance imaging (rs-fcMRI), we, the current and former graduate students, postdoctoral researchers, faculty colleagues, and academic friends, dedicate this two-issue special Festschrift publication series to him. We begin this publication with some personal reflections about Jim's impact on our scientific careers and the broader academic discipline of functional neuroimaging. More personal reflections were included in the first issue of this Festschrift series.

Jim Hyde's Former Graduate Students

When asked by the editors to write an article to celebrate Dr. James Hyde's contribution to the field of MRI research, I thought that it would only be fitting for me to write something related to high spatial resolution. I have an anecdotal story for this idea. When I was a first-year graduate student, I remembered distinctly that he had once posed a challenge to his students during a usual lunchtime journal club: ''Whoever gives the best example for high spatial resolution would win the 'grand prize'—a Snickers chocolate bar.'' I gave what I thought was a wild example: ''How about reading a newspaper on this table but from outer space?'' He laughed, but then threw me the Snickers across the table. Today, perhaps reading a newspaper on Earth from space is almost a reality (thanks, Googlemaps!), but the improvement in MRI spatial resolution has not been as dramatic. I have devoted a significant portion of my research time to pursuing high spatial resolution, and recently, we have begun investigating the impact of high spatial resolution on imaging brain connectivity. In this special issue celebrating Dr. Hyde, I dedicate this article to him, for his wisdom and ingenuity have helped shape our research world. He has been a constant force in challenging while also encouraging his students and peers to innovate the methodology and pursue the scientific truth.

Allen W. Song, PhD
MCW Biophysics PhD, 1995
Professor and Director for Duke-UNC Brain Imaging and Analysis Center
Departments of Radiology, Neurobiology, Psychiatry and Behavioral Science, and Biomedical Engineering
Duke University

It was upon the occasion of an industry-job interview in Milwaukee that I dropped by the office of a famous physicist I had heard of, Dr. James Hyde, at the Medical College of Wisconsin. So inspiring was his broad grasp of not only physics but other fields, and how he brought that knowledge to bear on scientific questions, that I abandoned my industry aspirations and joined his lab as a doctoral student. I was not disappointed. Dr. Hyde always encouraged and challenged me to think of new ideas. He would then point out all the limitations and pitfalls, and together we would come up with a better idea that would make for a great experiment. Ultimately, however, what Dr. Hyde cared most about was the data. As long as we could reproduce our results, we were free to interpret them as we liked. In spite of his great scientific and entrepreneurial accomplishments, I have always felt that family is Dr. Hyde's top priority. Those of us fortunate enough to work with him are part of that family, which for me is a great honor.

Bharat Biswal, PhD
MCW Biophysics PhD, 1996
Professor and Chair
Department of Biomedical Engineering
New Jersey Institute of Technology
Founding Editor-in-Chief
Brain Connectivity

I organized this special Festschrift issue of *Brain Connectivity* to honor a great scientist, mentor, and colleague. James S. Hyde has made numerous contributions in his storied career, including being the senior author on the first published article describing blood oxygen level-dependent (BOLD) fMRI contrast in the human brain. More importantly for the readers of this journal, Dr. Hyde was the senior author on the first depiction of resting-state fcMRI. He has had a remarkable impact on the careers of a multitude of individuals in the biophysics and medical imaging communities. My own journey through Dr. Hyde's lab started the same way as every other former student of his: with a meeting in his office. Before that meeting, I had called Dr. Hyde on the phone with some crazy idea about the possibility of building a low-field MR animal scanner from scratch. It was the type of project that someone of Dr. Hyde's stature could easily dismiss, especially given my clear ignorance of the size and complexity of the project. Dr. Hyde politely listened and patiently answered my questions and invited me to his office. As I sat in the now-familiar office, with Jim gently reclining in his chair, we discussed my future. With keen abilities in mentor jujitsu, Jim was able to redirect my ambition in the direction of a more feasible project. In about an hour, Dr. Hyde had outlined the project that would form the nucleus of my PhD thesis, as well as several additional projects that could have easily started the careers of 10 other PhD students. I had come to Jim at a difficult point in my life, and I had just spent a year rotating through several other laboratories at MCW without finding a home. At the end of our first meeting, Jim said something to me that set the tone for our future academic relationship and made a lasting impact on my opinion of him. Dr. Hyde said with a firm handshake: ''I will be straight with you,

and I want you to be straight with me.'' Since that meeting we have both kept that promise.

Dr. Hyde lives in the world of ideas. His former students have all gone on to successful scientific careers because of his remarkable mentoring ability. Jim gives his students enormous latitude to develop their own research projects within his wide boundaries. Dr. Hyde's main role as advisor is to serve as a never-ending fountain of original thought, and he relishes the opportunity to sit in his office with a student that is stuck, working logically through the problem. Arguments and vigorous discussion are encouraged, and Dr. Hyde doesn't want his students to be gentle flowers and always agree with him. Jim is a true scientist. He rewards creativity and the pursuit of the truth. There are many phrases and lessons Jim offers that stay with me in my own career. Phrases such as ''The data is the data'' (i.e., believe your data), and lessons such as when there is conflict always bring the conversation back to the science and stay out of the politics, have had a great impact on me as a researcher. Jim has a tremendous ability to assemble a diverse team of investigators, identify everyone's talent and area of expertise, and then mold the project based on the team's strengths and weaknesses. Scientists can be difficult, arrogant, and sluggish. In spite of this, I had no trouble finding contributors to this special Festschrift issue, and many people contacted me without any notice. This is a testament to Jim's scholarly reputation, congenial demeanor, and admiration by his former students, coworkers, and colleagues. It is astounding for me to daily sit in that now-familiar office and have the same type of wide-ranging scientific conversation as the one I had upon first meeting Dr. Hyde many years ago. On behalf of Jim's former students, I wish Dr. Hyde many additional years to his now-celebrated career and hope that he enjoys his special Festschrift issue of *Brain Connectivity*.

Christopher Pawela, PhD
MCW Biophysics PhD, 2008
Assistant Professor
Department of Plastic Surgery
Medical College of Wisconsin
Founding Editor-in-Chief
Brain Connectivity

My research career began during a lunch conversation with Dr. James Hyde. Likewise, I am fairly certain that Dr. Hyde's research career in MRI began with the same conversation. The difference was that I was an inexperienced biomedical engineer-turned medical student completing my first year of medical school at the Medical College of Wisconsin. Professor Hyde was a distinguished professor and the director of the National Biomedical Electron Spin Resonance (ESR) Center at the Medical College of Wisconsin with more than two decades of demonstrated creativity, scholarship, and success in the field of electron spin resonance.

It was the spring of 1983, and I was looking for a summer job. During the previous summer of 1982, I had completed a cooperative engineering internship at GE Medical Systems, and I was fortunate to work with a team of people who were developing GE's first 1.5 T MRI scanner. Somehow I learned of new technology that had been created in ESR, something called the loop–gap resonator that Hyde and his research team were using to improve the signal-to-noise ratio in their experiments. The only thing I knew about the ESR field was that both nuclear magnetic resonance (NMR) and ESR shared the word ''resonance,'' and fortunately for me, Jim agreed to spend a few moments explaining what he was doing. Of course he was already aware of Lauterbur's proposal to create NMR images, and like he has demonstrated throughout his career, he was unafraid to jump into the water, confident that he could contribute something valuable to NMR imaging. I asked whether we could use the loop–gap technology to improve the signals in NMR imaging, and he essentially said, ''Well that sounds interesting; let's give it a try.'' He immediately described to me a vision for using the coil technology to improve signal strength and detail in NMR imaging using local coils. By the end of our sandwiches, I think, his mind had already moved about 3 years ahead, which was about the time required to see his ultimate vision for surface coil technology carried out. Jim agreed to sponsor my application to an NIH summer research fellowship to explore the loop–gap resonator technology for P-31 NMR spectroscopy, and so our work together in the development of coils for magnetic resonance spectroscopy and MRI began. I am proud of the fact that our lunchtime conversation also began Jim's amazing second career in the development and application of MRI technology for imaging, including his seminal contributions to MRI coils, imaging methods, fMRI of the brain, and his work in connectivity.

Jim's support taught me the value of embracing the thoughts of a young person who really doesn't know any better and mentoring that naivety into something useful. Jim also demonstrated to me the value of the horizontal sharing of ideas and his fearlessness in taking the plunge into new waters, knowing that he is fully capable of contributing new ideas to whatever pond in which he chooses to swim.

Thomas Grist, MD
Professor and Chair
Department of Radiology
University of Wisconsin–Madison

Jim Hyde's Current and Former Colleagues from the Medical College of Wisconsin

When I began as a graduate student at the Medical College of Wisconsin in the early 1990s, there was a very strong culture of hardware development within the Biophysics Research Institute, and it was clear to everyone that Jim Hyde was the driving force behind that culture. As a beginning graduate student, I did not have a full appreciation of how privileged I was to work in an environment where hardware development was encouraged, taught, and respected. It is more akin to an art passed on from master to apprentice than a skill taught in a classroom, and there are so few masters who still teach the craft.

At MCW, in Biophysics, it was understood that every graduate student would build either an RF coil or a gradient coil, or ideally, one of each. Jim had all of the necessary support structures in place to help us realize our designs: RF engineers, an experienced machinist, and complete machine

and electronics shops. Since I had an innate love of electronics since I was very young, I relished the opportunity to build and test my own medical devices.

But even more important than having all the requisite support, Jim had created an environment where students felt comfortable taking risks with their designs. I now recognize, as a PI with my own lab, creating such an environment is critical to discovery and innovation. I lost track of how many capacitors I blew testing my RF coils, and I still cringe when I remember the error message I received when my first gradient coil caused feedback, blowing a gradient amplifier. But apart from making sure I knew what caused my errors, Jim never severely admonished me because he knew that if he did, I would pull back and be fearful of pushing those limits: too afraid to attempt something that had never before been attempted. I take this pioneering spirit with me in all aspects of my professional career, and I believe it's one of the most important gifts I can pass on to my own students.

Mary Elizabeth Meyerand, PhD
MCW Biophysics PhD, 1996
Professor
Departments of Medical Physics
and Biomedical Engineering (Chair)
University of Wisconsin–Madison

By the time I met Jim as a graduate student in 2004, his prevalence in the history of electron spin resonance, functional MRI, and resting-state functional connectivity had already been cemented and cured, but his curiosity had not been quenched. His passion for developing novel technology to further enhance the information content in BOLD data has been contagious, and his desire to share insights with a young investigator has been instrumental to the formation of my lab. The realization of enhanced information content in resting-state acquisitions that is available with minor adjustments to a standard EPI acquisition sequence, described in this issue in an article I wrote with one of Jim's former students, is one such insight that arose from an informal conversation in the halls of MCW. Other conversations we've had in the last 10 years have led to a wealth of further ideas, which, as most who have talked with Jim would know, could fill numerous scientific careers with appropriate and deserving study. That is arguably Jim's most significant contribution to the field: The large number of scientists who claim Jim as a mentor and who have developed full research programs related to his tangential musings has shaped the field of functional neuroimaging in the last few decades and will continue to do so in the foreseeable future.

Andrew S. Nencka, PhD
MCW Biophysics PhD, 2009
Assistant Professor
Department of Biophysics
Medical College of Wisconsin

Jim Hyde: scientist, mentor, inspiration

My first encounter with Jim Hyde was in late 1991 when a colleague came to me with the Belliveau Science article about fMRI in hand and said, ''I think there are guys here at the Medical College of Wisconsin that might know something about this. Let's go talk to them!'' Upon approaching Jim about this new exciting development, he responded in his typical low-key manner with a big grin: ''Oh sure, I've got two students, Wong and Bandettini, who can do the same thing, but they don't have to use a contrast agent! Why are *you* interested?''… and as they say, the rest is history. Within weeks we had demonstrated visual cortex activation and in the summer of 1992, started writing an NIH grant to fund research into applications of fMRI. This scenario became a template for my personal experiences with Jim Hyde. Some new development, large or small, would almost always be the first thing out of his mouth upon encountering him in the hall or at some meeting. This would often trigger a sequence of novel ideas and applications from me as the potential implications of the innovation would ''sink in,'' but the subsequent refinement of those nascent ideas is what I appreciated most. Jim would always cut directly to the most fundamental principles operating at the heart of any technological innovation or tech application. As I encountered this trait of his each time, I began to try to emulate his thought process myself, always trying to look deeper into a problem for the most fundamental issues, and then not shying away from a spirited ''argument'' about which ideas held water and which didn't. At our institution, spirited discussions between Jim and any of the faculty, staff, or students became an ''event'' that was wholly appreciated by some for the intellectual stimulation and honesty they evoked but were likely feared by others who weren't prepared to defend an idea or give it up! As I look back over the decades of my experiences with Jim, it is this characteristic of uncompromising scientific curiosity, rigor, and insight that I most appreciate and that, I hope, in some way have made me a better scientist.

Edgar A. DeYoe, PhD
Professor
Department of Radiology
Medical College of Wisconsin

Jim has always served as a fabulous mentor and role model for me during my academic research career. I specifically learned strategies from him on how to harmonize individual research interests with the goals of federal funding agencies. His vision, energy, and motivation related to scientific discovery and technological advancement will continue to enhance the Medical College of Wisconsin Center for Imaging Research.

Shi-Jiang Li, PhD
Professor and Director, Center for Imaging Research
Department of Biophysics
Medical College of Wisconsin

Jim Hyde has been a tremendous colleague and mentor to me. I remember that the first time I met Jim was at the MCW Biophysics holiday party in December 2000 when I was interviewing for an assistant professor position. I was instantly struck by his tremendous knowledge of fMRI. Having been an MCW faculty member since then, I have had many substantive interactions with Jim. I have to admit, it wasn't until years later that I fully understood what he was describing. Over the years, I have repeatedly witnessed his incredible insight into MR physics and fMRI analysis. My knowledge and

understanding has grown with each and every discussion with Jim. Without Jim, I would not be where I am today. So I would like to personally thank him for his mentoring. The fMRI field has been changed because of his presence.

Daniel B. Rowe, PhD
Professor and Head of Functional Magnetic Resonance Image Analysis Lab
Department of Mathematics, Statistics, and Computer Science
Marquette University

A Japanese saying points out that a true master can be identified from his students. In the case of Jim Hyde, this recognition is very easy; just look how Jim's students have performed in the relatively demanding neuroimaging field alone. They have become professors, distinguished editors-in-chief of several important publications, leading scientists, and pioneers.

I have had the honor to witness Professor Hyde's scientific endeavor at MCW, and he has helped me in difficulties that inevitably arise when dealing with completely new phenomena related to spontaneously active brain. One example of his fearless attitude was a chat in Miami for ISMRM where Professor Hyde said: ''Well, the resting-state stuff was much more exciting while it was still controversial!'' I personally could have dealt with less excitement and turmoil during those days, but a true master stands smiling in the midst of the storm. That's Jim Hyde for you.

Vesa Kiviniemi, MD, PhD
Neuroradiologist and Adjunct Professor
Department of Diagnostic Radiology
University of Oulu
Finland

I will always be grateful to Jim Hyde for giving me a job and changing my career drastically (for the better). I showed up in Milwaukee in Spring 1993 looking for a position there and somehow impressed him enough to go sweet-talk some money from the dean and to give me a chance. I didn't know anything at all about NMR, MRI, or fMRI, and the first 6 months were a desperate scramble to learn a lot of new science and also to contribute something. Jim Hyde was very supportive and brimming over with ideas—one of the things for which I admire him. When I came up with my plans for AFNI and real-time fMRI, he basically said ''go for it,'' and so I did. His ability to find talented people and launch them to do solid work, nudging with his free-ranging notions from time to time, is yet another thing that I admire him for.

Robert W. Cox, PhD
Director
Scientific and Statistical Computing Core
Division of Intramural Research Programs
National Institutes of Health, Public Health Services

The first reflection that comes to mind is his enormous scientific and methodological contributions to the fields of EPR, NMR, MRI, fMRI, real-time fMRI, and fcMRI. When I came to the Biophysics Research Institute as a postdoc in late 1997, I was really impressed and even imprinted by the wonderful research and intellectual environment Jim had created there. I think it is fair to say that in addition to bright ideas, science also requires enormous drive on many levels to establish and sustain a thriving research environment. In addition to being an extraordinary scientist, Jim quite remarkably was able to establish and sustain such a research environment, mostly because of his can-do attitude. Discussions with Jim are especially interesting because of his ''hard pulse'' questions with a ''wide spectrum'' of content. Conversations with Jim frequently took place during the long walks along the hallway from the exit door back to his office and the other way around. I think the physical activity improved our blood flow (especially mine) and helped answer Jim's concerns. Now an almost scary reflection: it was early 1998 I think, and a local head gradient coil had broken. Unfortunately, it happened during my 3 T experiments with single-slice EPI scanning and with TR = 54 ms. At the time, that was the only gradient coil available for all fMRI studies at MCW, and my walking discussions with Jim stopped for a few weeks until the replacement coil was built. The most important things I have learned from Jim Hyde (so far), and I am very grateful for, are that you don't know everything; always ask questions; persist in research; persist in seeking funding; don't be afraid to take aim on new, unknown, and unfamiliar things; don't be afraid to take risks; and learn from failures.

Jerzy Bodurka, PhD
Chief Technology Officer at the Laureate Institute for Brain Research
Associate Professor
College of Engineering
University of Oklahoma

Jim Hyde's Friends and Colleagues Outside of the Medical College of Wisconsin

I have had many years of friendship with James Hyde. In the late 1960s, I recall that I went to interview for a job at Varian, but by that time Jim had already left. Because of my work in the field of EPR study in those days, I had a great respect for him. Since then, both of us went to the field of MR, or MRI, to fMRI. It was always a pleasure to see him, as well as his wife, Karen, at annual meetings of SMRM/ISMRM.

When I visited Milwaukee to hear the thesis presentation by his student Peter Bandettini, the topic was on fMRI. I was lucky that I had a chance to show our fMRI results before Peter's thesis defense presentation.

We saw the paper on the first observation of resting-state signal correlation by Bharat Biswal when we were working on the time series of MRI data. We thought the slow MRI oscillation was due to vaso-motion in spite of Jim's warning that the phenomena were neuronal. As everyone knows nowadays, their finding in 1995 was the most important milestone in the neuroimaging world.

I wish to convey to Jim my admiration of him for his many important contributions to the MR field, as well as my appreciation of the warm friendship.

Seiji Ogawa, PhD
Visiting Professor and Director of fMRI Research
Neuroscience Research Institute
Gachon University of Medicine and Science
Korea

Jim Hyde is impressive in the quality of science he has produced, in intellect, in stature, and, most importantly for many of us, in his generosity in supporting the good science of others. I first met Jim in the early 1980s when he came to visit Mel Klein's laboratory at UC Berkeley/Lawrence Berkeley Laboratories.

I had the great honor of being a graduate student of Mel's. Mel and Jim had similar trajectories as scientists. Trained as physicists, both began their careers in the formative years of magnetic resonance in California; Jim at Varian and Mel at Livermore and then Lawrence Berkeley Laboratories. Both turned their spins to studying protein structure and function in the mid to late 1960s. Both were extremely knowledgeable about physics and biophysics. In Mel's lab there were students working on NMR, EPR, fluorescence, and XAFS. Indeed, the environment Jim created at the Medical College of Wisconsin embodied the three pillars found only in the very best biophysics labs: challenging problems, strong theory, and superb instrumentation development all in one group! Thus, it was no surprise to many of us when Jim's group quickly had major impacts in MRI after deciding to enter the MRI field.

The reason for the visit to the Berkeley lab was for Mel and David Britt to pick Jim's brain about loop–gap resonators. This was a creative new EPR detector design that Jim had developed (thus, no surprise Jim would go on to impact MRI coil design as well). I knew Mel had great respect for Jim because for my first project in his lab, Mel handed me Jim's EPR papers that used saturation transfer to study rotational motion and suggested there must be an analogy for NMR to study phospholipid head group rotation. The depth of the respect only became clear as I noticed how much Dave and Mel were preparing for the visit. I spent only a few minutes talking with Jim about my own project, which had evolved, thanks to Michael Weiner's influence, to using 31P NMR saturation transfer to study enzyme kinetics in rat heart and kidney. I got to know Jim much better when Chien Ho had him join the advisory committee for our NIH-funded Regional Resource at Carnegie Mellon University. Chien Ho was another early 1960s pioneer of magnetic resonance who studied important biological problems and thus knew Jim well. Chien picked his advisory committees very, very carefully, and Jim was at the top of his list. This was during the early stages of my own laboratory, and Jim had only recently acquired a 3 T MRI at Medical College of Wisconsin. During those years, I came to better appreciate Jim's depth of insight and creativity. However, most important were the positive suggestions and the generous support he showed for my own work. For this I will be forever grateful.

Alan Koretsky, PhD
Senior Investigator
National Institute of Neurological
Disorders and Stroke (NINDS/NIH)

My first close encounter with Jim was perhaps at the fMRI workshop held in Arlington, VA, in 1993. Since then, I have met him multiple times, either during my visits to Milwaukee or at meetings and workshops. What I found special about Jim is that despite being such a legend in the field, he is really down-to-earth, easy to approach, and open for candid and frank exchanges. Besides his major contributions to EPR, his contributions to and impact on MRI include leading the work that brought about one of the first papers on fMRI and the work that discovered resting-state functional connectivity. It is fair to state that our field would not be as it is today without Jim. On a personal note, I have always enjoyed many chats with him, and my work has benefited significantly from his inspiration, insight, and wisdom.

Xiaoping Hu, PhD
Professor and Director
Biomedical Imaging Technology Center
Department of Biomedical Engineering
Emory University

I met Jim Hyde when I was at the University of Minnesota's Center for Magnetic Resonance Research in early 1990, and we were directly competing in fMRI research at that time. Since then, I have followed his research and visited Milwaukee many times. He has superb keen insights into science and has produced many seminal papers. His research in functional neuroimaging is crucial, especially as resting-state fMRI opens a new window for visualizing brain functions and connectivity. I do believe that one of the most important contributions to the scientific field is mentoring young scientists. Jim has trained so many leading scientists, and I wish my son went to his lab as a graduate student. Our entire MRI field tremendously benefits from his leadership, science, and education, and he is my role model. Jim, be healthy and keep producing excellent papers and good scientists.

Seong-Gi Kim
Director and Professor
Departments of Global Biomedical
Engineering and Biological Sciences
Center for Neuroscience Imaging Research,
Institute for Basic Science
Sungkyunkwan University (SKKU)
Korea